

REMARKS

Claims 1, 2, 4, 26, 30, 39, 42, 73, 74, and 78-83 are pending as claim 76 has been cancelled. Claim 1 has been amended to clarify that the inhibitor binds to Ena/VASP. Support for the amendment can be found at least in claim 2 as originally filed and at page 8, lines 18-19. Claim 42 has been amended to remove a duplicate word “the” that was inadvertently included in the claim as filed. No new matter has been added.

Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 1, 2, 4, 73, 74, and 76 under 35 U.S.C. §112 as containing new matter. Applicants have amended claim 1 to clarify that the inhibitor binds to Ena/VASP, which is supported by the specification as filed. Applicants submit that the amendment obviates that basis for the rejection of claims 1, 2, 4, 73, and 74 and respectfully request that the Examiner withdraw the rejection of claims 1, 2, 4, 73 and 74 under 35 U.S.C. §112.

The Examiner rejected claims 1, 2, 4, 26, 30, 39, 42, and 73-74, 76, and 78-83 as lacking enablement under 35 U.S.C. §112. Applicants traverse the rejection.

The Examiner states that the specification is enabling for a method for inhibiting cytoskeletal actin rearrangement in a T cell or a platelet, a method for inhibiting a T cell response and a method for increasing platelet aggregation comprising contacting the T cell or platelet with an amount of a Fyb/SLAP complex inhibitor sufficient to inhibit the formation of a complex of an Ena/VASP protein and a Fyb/SLAP protein, wherein the Fyb/SLAP inhibitor it EVH1 binding peptide FPPPP (SEQ ID NO:15), but contends that the specification is not enabling for “any Fyb/SLAP complex inhibitor that binds Fyb/SLAP or Ena/VASP proteins sufficient to inhibit the formation of a complex of an Ena/VASP protein and a Fyb/SLAP protein in claim 1”. Applicants have amended claim 1 as described above to clarify that the Fyb/SLAP complex inhibitor binds Ena/VASP protein. Applicants submit that the specification is enabling for Fyb/SLAP complex inhibitors that bind Ena/VASP and inhibit the formation of a complex of an Ena/VASP protein and a Fyb/SLAP protein and the amendment obviates the basis for the rejection of claim 1.

The Examiner also contends that the claims fail to meet the enablement requirement for

the “how to make” prong of the U.S.C. 112 1st paragraph. The Examiner states that the “artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claim and consequently would not know how to make them”. Applicants disagree with the Examiner’s conclusion and assert that a representative number of compounds that fall within the scope of the claim are provided in the specification as filed.

Applicants respectfully assert that a representative number of inhibitors are described at page 8, line 18 through page 9 line 6 of the specification as filed. The specification describes the inhibitor comprising SEQ ID NO:5 (FPPPP) as well as additional inhibitors such as: Act A repeats, EVH1 binding peptides, ScarWA, and dominant negative Fyb/SLAP fragments. Preferred inhibitors described in the specification include molecules having at least one acidic amino acid on one or both sides of the FPPPP sequence, and “reverse change variants” having at least one basic amino acid on one or both sides of the FPPPP sequence. Additional inhibitors include EVH1 domain containing proteins, Ena/VASP fragments, and antibodies or antibody fragments that bind Fyb/SLAP protein or Ena/VASP protein. The person of skill in the art is familiar with each of these known molecules. Applicants also provided inhibitors that are mimetics for the FPPPP peptide, i.e., they compete with FPPPP for binding to the EVH1 domain. Thus, Applicants submit that the identities of a representative number of inhibitors are provided in the specification as filed and that the examples are at least adequate to enable the methods of the invention as claimed.

Accordingly, in view of the claim amendments and reasoned statements provided above, Applicants believe the claims to be enabled throughout their scope and respectfully request that the Examiner withdraw the rejection of claims 1, 2, 4, 26, 30, 39, 42, 73, 74, and 78-83 under 35 U.S.C. §112, first paragraph.

The Examiner rejected claims 1, 2, 4, 26, 30, 39, 42, and 73-74, 76, 78-83 under 35 U.S.C. §112, first paragraph as lacking adequate description. Applicants have amended claim 1, as described above, and believe this amendment clarifies that Applicants were in possession of the claimed methods at the time of filing.

The basic requirement of the written description requirement is that the claimed invention must be described clearly enough to allow one of ordinary skill in the art to recognize that the

inventors invented the claimed invention. Vas-Cath v. Mahurkar 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991); Lockwood v. American Airlines, Inc. 107 F.3d 1565, 41 USPQ2d 1961 (Fed. Cir. 1997); In re Gosteli 872 F.2d 1008, 10 USPQ 2d 1614 (Fed. Cir. 1989). The requirement is based on the knowledge of the skilled artisan in the particular art: the Applicant must convey to one of ordinary skill in the art through the disclosure in the invention that the applicant was in possession of the claimed invention.

The Examiner asserts that Applicant has not provided sufficient information regarding the identity of Fyb/SLAP complex inhibitors, inhibitors that bind to the EVH1 domain or peptide mimetics other than the proline-rich peptide FPPPP (SEQ ID NO:15). Applicants respectfully point out that the specification as filed does provide numerous examples, in addition to SEQ ID NO:15, of molecules that are known Fyb/SLAP complex inhibitors. These Fyb/SLAP inhibitors are clear examples of molecules that inhibit the formation of a complex of a Fyb/SLAP protein and an Ena/VASP protein. Applicants contend that molecules that are useful to inhibit the complex formation are clearly described and that the identification of such inhibitors in the specification as filed, along with the teaching provided would be sufficient for one of ordinary skill in the art to use a variety of Fyb/SLAP complex inhibitors in the methods of the invention. Applicants respectfully assert that the examples of Fyb/SLAP complex inhibitors that are provided in the specification as filed are known molecules, and that Applicants indicate through the teaching in the application as filed that these molecules are members of a genus of molecules that are useful in the claimed methods.

The Examiner states in Paragraph 9 of the Office communication mailed December 3, 2003, that the “Applicants admit that the specification does not provide numerous examples of Fyb/SLAP complex inhibitors because the claimed invention relates to the use of such agents, and is not claim to the agents themselves.” Applicants disagree with the Examiner’s reading of Applicant’s statements in the responses filed on 6/13/03 and 8/12/03 (with the RCE). In each response, Applicants indicated that ““it is not necessary for Applicants to describe each and every Fyb/SLAP complex inhibitor” and “Although Applicants do provide numerous examples of Fyb/SLAP complex inhibitors in the specification, Applicants contend that because the claimed invention relates to the use of such agents, and is not a claim to the agents themselves, Applicants need not describe or further identify additional members of the universe of Fyb/SLAP

complex inhibitors, but only must adequately describe the claimed methods in such a way as to allow one of ordinary skill in the art to recognize that Applicants were in possession of the claimed methods at the time of filing.” Thus, contrary to Examiner’s statement in support of the rejection, Applicants did not admit that the specification does not provide numerous examples of Fyb/SLAP complex inhibitors. To the contrary, Applicants have provided a number of examples of Fyb/SLAP inhibitors in the specification as filed and respectfully assert that the skilled artisan would clearly recognize from the specification and Examples that Applicants were in possession of the claimed invention of using agents that are Fyb/SLAP complex inhibitors. Applicants respectfully submit that a skilled artisan would be able to recognize that Applicants were in possession of the claimed methods at the time of filing.

Applicants respectfully request that the Examiner withdraw the rejection of claims 1, 2, 4, 26, 30, 39, 42, and 73, 74, and 78-83 under 35 U.S.C. §112.

Rejections Under 35 U.S.C. §103

The Examiner rejected claims 1, 2, 4, 26, 30, 73-74, 76, and 78-80 under 35 U.S.C. 103(a) as being unpatentable over Niebuhr et al. (EMBO Journal 16:5433-5444, 1997) in view of Krause M. (<http://www.bilbl.io.tu-bs.de/ediss/data/20000203a/20000203a.html>, Feb. 1999). Applicants traverse the rejections.

It is not clear from the Office Action why one of ordinary skill in the art would have been motivated to combine and modify the teachings of the cited prior art to reach the claimed invention. The Examiner has not provided an explanation of the motivation to modify and the motivation to combine the modified teachings that one of ordinary skill in the art would have had in making the changes required to produce the claimed invention.

The requirement for a specific motivation to combine and modify the teaching of the prior art references was most recently set forth by the Court of Appeals for the Federal Circuit in In re Sang Su Lee. Applicants provide below an excerpt for the convenience of the Examiner.

When patentability turns on the question of obviousness, the search for and analysis of the prior art includes evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the references relied on as evidence of obviousness. See, e.g., McGinley v. Franklin Sports, Inc., 262 F.3d 1339, 1351-52, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001) (“the central

question is whether there is reason to combine [the] references," a question of fact drawing on the Graham factors).

"The factual inquiry whether to combine references must be thorough and searching." Id. ***It must be based on objective evidence of record.*** This precedent has been reinforced in myriad decisions, and cannot be dispensed with. See, e.g., Brown & Williamson Tobacco Corp. v. Philip Morris Inc., 229 F.3d 1120, 1124-25, 56 USPQ2d 1456, 1459 (Fed. Cir. 2000) ("a showing of a suggestion, teaching, or motivation to combine the prior art references is an 'essential component of an obviousness holding'") (quoting C.R. Bard, Inc., v. M3 Systems, Inc., 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed. Cir. 1998)); In re Dembiczak, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references."); In re Dance, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998) (there must be some motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant); In re Fine, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988) ("teachings of references can be combined only if there is some suggestion or incentive to do so.") (emphasis in original) (quoting ACS Hosp. Sys., Inc. v. Montefiore Hosp., 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984)).

The need for specificity pervades this authority. See, e.g., In re Kotzab, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000) ("particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed"); In re Rouffet, 149 F.3d 1350, 1359, 47 USPQ2d 1453, 1459 (Fed. Cir. 1998) ("even when the level of skill in the art is high, the Board must identify specifically the principle, known to one of ordinary skill, that suggests the claimed combination. In other words, the Board must explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious."); In re Fritch, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (the examiner can satisfy the burden of showing obviousness of the combination "only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references").

In re Sang Su Lee, slip op. 7-9 (Fed. Cir. 2002) (emphasis added except where noted)

The Examiner stated that the motivation to combine the references is that "one of ordinary skill in the art would have a reasonable expectation to make the claimed invention "to examine the biological consequence of specifically eliminating the EVH1 binding sites from the ActA protein" and to "target the inhibition of the VASP with FPPP in a method of inhibiting a T cell response to T cell receptor stimulation" Office Action at page 8.

Respectfully, these bases for motivation fall far short of the standard required by the law. The motivation is not "based on objective evidence of record" as is required. Id. In the Sang Su Lee case, the use of conclusory statements like those used by the Examiner in this case were criticized by the Federal Circuit as improper:

With respect to Lee's application, neither the examiner nor the Board adequately supported the selection and combination of the Nortrup and Thunderchopper references to render obvious that which Lee described. The examiner's conclusory statements that "the demonstration mode is just a programmable feature which can be used in many different device[s] for providing automatic introduction by adding the proper programming software" and that "another motivation would be that the automatic demonstration mode is user friendly and it functions as a tutorial" do not adequately address the issue of motivation to combine. This factual question of motivation is material to patentability, and could not be resolved on subjective belief and unknown authority. It is improper, in determining whether a person of ordinary skill would have been led to this combination of references, simply to "[use] that which the inventor taught against its teacher." W.L. Gore v. Garlock, Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983). Thus the Board must not only assure that the requisite findings are made, based on evidence of record, but must also explain the reasoning by which the findings are deemed to support the agency's conclusion.

Id. at 9.

The Examiner also did not analyze the level of skill in the art as is required for a proper analysis of obviousness. Graham v. John Deere Co., 383 US 1, 17, 148 USPQ 459, 467 (1966) . The Examiner introduced no evidence and provided no analysis regarding a person of ordinary skill in the art. Consequently one of the factual inquiries required for a determination of obviousness has not been addressed at all by the Examiner. Graham, 383 US at 17, 148 USPQ at 467. One cannot provide objective evidence of the motivation of one of ordinary skill in the art if one does not articulate the level of skill in the art.

In connection with this requirement, the court in In re Sang Su Lee further held:

The determination of patentability on the ground of unobviousness is ultimately one of judgment. In furtherance of the judgmental process, the patent examination procedure serves both to find, and to place on the official record, that which has been considered with respect to patentability. The patent examiner and

the Board are deemed to have experience in the field of the invention; however, this experience, insofar as applied to the determination of patentability, must be applied from the viewpoint of "the person having ordinary skill in the art to which said subject matter pertains," the words of section 103. In finding the relevant facts, in assessing the significance of the prior art, and in making the ultimate determination of the issue of obviousness, the examiner and the Board are presumed to act from this viewpoint. Thus when they rely on what they assert to be general knowledge to negate patentability, that knowledge must be articulated and placed on the record. The failure to do so is not consistent with either effective administrative procedure or effective judicial review. The board cannot rely on conclusory statements when dealing with particular combinations of prior art and specific claims, but must set forth the rationale on which it relies.

Id. at 12.

The Examiner has not set forth a rationale to specifically explain the motivation of one of ordinary skill in the art in combining the references asserted to render the claimed invention obvious. Thus a proper obviousness rejection has not been made and it should be withdrawn.

Based on the foregoing arguments, Applicants respectfully request that the Examiner withdraw the rejection of the claims under 35 U.S.C. §103.

The Examiner rejected claims 39, 42, 81-83 as being unpatentable over Niebuhr et al. (EMBO Journal 16:5433-5444, 1997) in view of Krause M. (<http://www.bilblilio.tu-bs.de/ediss/data/20000203a/20000203a.html>, Feb. 1999) as applied to claims 1-2, 4, 26, 30, 73-74 and 78-80 above, and further in view of Aszodi et al. (EMBO Journal 18:37-48, 1999). Applicants respectfully traverse the rejection.

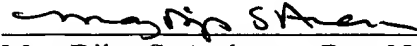
Based on the arguments presented above regarding the rejection of claims 1, 2, 4, 26, 30, 73-74, 76, and 78-80 under 35 U.S.C. 103(a) as being unpatentable over Niebuhr et al. in view of Krause M., Applicants submit that the Examiner has not set forth a *prima facie* case to support the rejection of claims 1, 2, 4, 26, 73, 74 and 78-80. Applicants respectfully request that the Examiner withdraw the rejection of the claims under 35 U.S.C. §103.

In view of the foregoing, Applicants respectfully request that the Examiner withdraw the rejections and act favorably upon the claims. If the Examiner requires clarification for any aspect of this response, or if prosecution can be expedited for any other reason, Applicants respectfully request that the Examiner contact the undersigned by telephone.

of this response, or if prosecution can be expedited for any other reason, Applicants respectfully request that the Examiner contact the undersigned by telephone.

Respectfully submitted,

Matthias Krause et al., Applicant



Mary Dilys S. Anderson, Reg. No. 52, 560

Wolf, Greenfield & Sacks, P.C.

600 Atlantic Avenue

Boston, MA 02210

Tel. (617)720-3500

Docket No. M00656.70065.US

Dated: June 3, 2004

X06/3/04x